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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/544,293	08/03/2005	Gerhardus Wilhelmus Lucassen	PHNLO30120US	1526
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EXAMINER ELHASSAN, AHMED A				
ART UNIT 4138		PAPER NUMBER		
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/544,293

**Applicant(s)**

LUCASSEN ET AL.

**Examiner**

AHMED ELHASSAN

**Art Unit**

4138

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08/03/2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SF/08)  
Paper No(s)/Mail Date 08/03/2005
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_

**DETAILED ACTION**

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention; it is unclear whether predetermined diameter value is 15 um or 10 um.

***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 3, 4, 7, 9, 16, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen et al. (WO02/057759) in view of Cook et. al (WO02/15786).

Regarding claim 1, Lucassen discloses a spectroscopic analysis apparatus (pp. 1, lines 8-9), for blood analysis (pp. 2, lines 20 – 21) comprising:

- an excitation system for emitting an excitation beam to excite a target region (pp. 1, line 10), and

- a detection system for detecting scattered radiation from the target region generated by the excitation beam and for analyzing the scattered radiation (pp. 2, line 8),  
Lucassen lacks only analyzing scattered radiation from blood in capillaries having a diameter below a predetermined diameter value

Cook teaches analyzing scattered radiation from blood in capillaries (pp. 8, lines 1-2 & "capillary plasma", col. 9, line 12) having a diameter below a predetermined ("small vessels", pp. 9, line 9) diameter value ("diameter masks", pp. 8, line 18) and/or including an amount of red blood cells below a predetermined cell amount.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen with only analyzing scattered radiation from blood in capillaries having a diameter below a predetermined diameter value and/or including an amount of red blood cells below a predetermined cell amount, in order to detect shadows caused by larger vessels in the background image.

Regarding claim 2. Lucassen-Cook as applied to claim 1, further includes:

- a monitoring system for emitting a monitoring beam to image the target region (Lucassen; pp.1, line 12),  
- an image processing unit for processing the image of the target region and for selecting vessel areas in the image showing capillary vessels or vessel portions having a diameter below a predetermined diameter value (Cook ; "diameter mask", pp. 26 lines 8-12, pp. 28, lines 19-20) and/or including an amount of red blood cells below a predetermined cell amount, and

- a control unit (Cook ; pp. 12, line 1 & FIG. 8) for controlling the detection system to analyze only scattered radiation from the selected vessel areas (Cook; pp. 26 lines 8-11)

Regarding claim 3, Lucassen- Cook, as applied to claim 2, includes a means for enrichment of plasma signal contribution, by measuring plasma ("capillary plasma" pp.9, line 12) where hematocrit concentration signal is low.

Regarding claim 4 Lucassen- Cook, as applied to claim 2 further includes selection means (Cook; abs., KPG algorithm) for a selective analysis of the plasma component (Cook; pp. 9, lines 10-12).

Regarding claim 7, Lucassen- Cook, as applied to claim 2, includes an image processing unit adapted for selecting vessel areas in the image showing capillary vessels or vessel portions including an amount of red blood cells below a predetermined cell (pp. 28, lines 27-28) amount by use of the contrast in the image (page 8, ,line 7).

Regarding claim 9 Lucassen- Cook, as applied to claim 2, includes control unit is adapted for controlling the excitation system to excite only predetermined areas in the upper dermis, in particular by use of a penetration depth of less than 300  $\mu\text{m}$  ("confocal" & "0.25 mm", pp. 6, line 33 , pp. 7 line 2) .

Regarding claim 16, Lucassen- Cook, as applied to claim 1, further includes a radiation source to emit an output beam and an optical separation system to separate the monitoring beam and the excitation beam from the output beam (Lucassen; pp.5, lines 13-18).

Regarding claim 18, Lucassen- Cook, include a spectroscopic analysis method (Lucassen, pp. 7, line 18), comprising the steps of:

- emitting an excitation beam to excite a target region (Lucassen; pp. 1, line 10),
- detecting scattered radiation from the target region generated by the excitation beam (Lucassen; pp. 2, line 8), - analyzing the scattered radiation (Lucassen; pp. 2, line 10), wherein only scattered radiation from blood in capillaries having a diameter below a predetermined diameter value (Cook ; "diameter mask", pp. 26 lines 8-12, pp. 28, lines 19-20).

3. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook, further in view of Chaiken et al. (WO/2000/001295)

Regarding claim 5 Lucassen- Cook, as applied to claim 2 lacks means for stopping or slowing down the blood flow, in particular by pressure squeezing (pp. 4, lines 13-15).

Chaiken teaches a means for stopping or slowing down the blood flow, in particular by pressure squeezing (pp. 4, lines 13-15).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen- Cook with a means for stopping or slowing down the blood flow, in particular by pressure squeezing, in view of Chaiken, with the motivation to diagnostically contrast the spectra of the blood-deplete and blood replete region.

4. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook, further in view of Gao et al. article (A method for vessel tracking ....., IEEE, 2001)

Regarding claim 6 Lucassen- Cook, as applied to claim 2 includes an image processing unit adapted for selecting vessel areas in the image showing capillary vessels or vessel portions having a diameter below a predetermined diameter (see rejection of claim 2, above).

Lucassen- Cook lacks use of optical vessel tracking means.

Gao teaches an optical ("light", pp. 882 line 1) method of vessel tracking (pp. 882, section 2.3) for determining vessel diameter (pp. 883, section 2.4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen-Cook with an optical method of vessel tracking, to select capillary vessels or vessel portions having a diameter below a predetermined diameter for analysis, with the motivation to provide robust vessel width estimation even in presence of noise.

5. Claims 8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook further in view Winchester et al (US 7,113,817).

Regarding claim 8, Lucassen- Cook, as applied to claim 2, lacks an image processing unit is adapted for retrieving velocity and distance information of red blood cells in the image and wherein the control unit is adapted for controlling the detection system by use of said velocity and distance information.

Winchester teaches an image processing unit adapted for retrieving velocity and distance information (FIG. 11, No. 110) of red blood cells (col. 14, line 31) in the image and wherein the control unit is adapted for controlling the detection system ("set gain"

FIG. 11, No. 94) by use of velocity and distance information (FIG. 11; feedback loop from No. 108 to No. 94).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen- Cook apparatus with an image processing unit adapted for retrieving velocity and distance information of red blood cells (in the image and wherein the control unit is adapted for controlling the detection system by use of velocity and distance information, with the motivation to prevent image pixel-saturation.

Regarding claim 10, Lucassen-Cook, as applied to claim 2, lacks a detection system adapted for retrieving intensity information from the scattered radiation and wherein the control unit is adapted for controlling the detection system by use of said intensity information (FIG. 11; feedback loop from No. 106 to No. 94).

Winchester teaches a detection system (FIG. 11, No. 94) adapted for retrieving intensity information ("Speckle contrast", FIG. 11, No. 106) from the scattered radiation and wherein the control unit is adapted for controlling the detection system ("set gain" FIG. 11, No. 94) by use of intensity information.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen- Cook apparatus with a detection system adapted for retrieving intensity information from the scattered radiation and wherein the control unit is adapted for controlling the detection system by use of intensity information, with the motivation to prevent image pixel-saturation

6. Claims 11, 12, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook and Couderc ( US 2004/0239924)



Regarding claim 11, Lucassen-Cook, as applied to claim 1, lacks a sample holding system comprising a capillary containing the blood to be analyzed. Couderc teaches a sample holding system (FIG. 3) comprising a capillary (FIG. 5, No. 202) capable of containing a laser-induced-fluorescence substance (e.g. blood) for biochemical analysis (pp. 1, [0001], line 4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen-Cook with a sample holding system comprising a capillary containing the blood to be analyzed, in view of Couderc with the motivation to save time and money by performing biochemical analysis without patient needing to be present.

Regarding claim 12, Lucassen-Cook, as applied to claim 11, includes capillary (No. 202 FIG. 4) adapted for moving along its longitudinal axis and/or along the direction of the incoming excitation beam (abs. lines 10-13).

Regarding claim 13, Lucassen-Cook, as applied to claim 11, includes means for causing a flow of blood through the capillary (FIG. 1; reservoir 32).

7. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook, further in view of Firkbank et al. (Experimental and Theoretical Comparison of NIR spectroscopy ....., 8750-7587/98, American Physiology Society)

Regarding claim 14, as understood for the purposes of this first office action, Lucassen-Cook apparatus as applied to claim 1, lacks that a predetermined diameter value is **less** than 15  $\mu\text{m}$ , in particular 10  $\mu\text{m}$ .

Firbank teaches (pp. 1916, lines 32-33) that hematocrit, i.e. also red blood cell concentration ratio, is lower in smaller capillaries.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen-Cook, with predetermining a smaller capillary diameter so as to attain minimum hematocrit ratio with the motivation to reduce the confounding hematocrit interference when measuring plasma concentration. It is known that minimum hematocrit ratio occurs when red blood cells form a single file when flowing through the capillary. It is also known that red blood cells (RBC) are 6-8 micrometer in diameter, so it would have been obvious that the maximum capillary diameter to attain a single RBC file is 15 micrometer.

8. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook and Firbank and further in view of Vadapalli (Calculation of Oxygen transport ....., Art. Cells, Blood Subs., and Immob. Biotech., 30(3), 157-188 (2002)).

Regarding claim 15 Lucassen-Cook, as applied to claim 1, lacks a predetermined blood cell amount is below hematocrit 0.35.

1) Firbank teaches (pp. 1916, lines 32-33) that hematocrit ratio is lower in smaller capillaries.

2) Vadapalli teaches a capillary hematocrit 0.35.

It would have been obvious to one of ordinary skill in the art, at the time of the invention, to modify Lucassen-Cook with 1) predetermining a hematocrit ratio with the motivation to analyze a smaller vessel, in view of Firbank, and 2) further modify Lucassen-Cook with particularly predetermining a hematocrit ratio below 0.35 with the motivation to specifically analyze capillaries in order to measure plasma concentration where hematocrit interference is reduced most.

9. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lucassen in view of Cook further in view of Chance (US 6,526,309)

Lucassen-Cook system as applied to claim 1 lacks a trigger means for triggering of the excitation system for time-resolved excitation of the target region

Chance teaches a trigger means for triggering of the excitation system (inherent in every excitation apparatus) for time-resolved excitation of the target region (col. 8, line 21).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify Lucassen-Cook, with a trigger means for triggering of the excitation system for time-resolved excitation of the target region, In view of chance with the motivation to also perform in-vivo trans-cranial examination of brain capillaries, in order to detect blood clots before causing a stroke.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AHMED ELHASSAN whose telephone number is (571)270-7390. The examiner can normally be reached on Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Melba Bumgarner can be reached on 571-272-4709. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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